

**REMARKS**

Favorable reconsideration of this application as presently amended is respectfully requested.

Applicants note, with thanks, the Examiner's acknowledgment of Applicants' election of Group 1, claims 1-27 that are under examination.

Applicants note, with thanks, the Examiner's observation "that this application appears to claim subject matter disclosed in provisional Application No. 60/156,946, filed November 9, 1999. A reference to the provisional application has been inserted at the first sentence of the specification of this application to rely on the filing date of the provisional application under 35 U.S. C. 119(e) or 120. See 37 CFR 1.78(a). However, the Oath/Declaration submitted fails to claim a benefit of priority to the provisional application." Thus, a Request for Priority is submitted herewith.

The Examiner has found the drawings filed with the application acceptable for examination purposes only. The drawings in this application are also objected to by the Draftsperson. Formal drawings with correction of noted defects, will be provided by Applicants, upon allowance of the application by the Examiner.

Applicants note, with thanks, the Examiner's indication that the references Zhao et al., Deandrade et al., and Zhi Z L have been considered only to the extent of their abstracts. The complete Zhao et al. reference is provided herewith for consideration in its entirety.

Claims 1 through 27 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With respect to claim 1, the improper antecedent basis problem has been obviated in the claims as currently presented.

The Office Action states “[c]laim 4 has improper antecedent basis problem in line 3 in reciting “a probe having a conical tip”. Applicants respectfully submit that the language of claim 4 is proper. Claim 4 is dependent on claim 2, which is dependent on claim 1. A “probe” is not mentioned in claim 2 or claim 1, hence “a probe” is correct usage in this context, and there is no antecedent basis problem present in claim 4.

The Office Action states “The term ‘high speed’ in claim 9 is a relative term which renders the claim indefinite. The term ‘high’ is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.” The term “high speed” is not present in claim 9 by itself, but rather is part of the phrase “high speed multi-sample tube” as defined in the specification. The term “high speed multi-sample tube” refers to any tube that may be used with a peristaltic pump that has compression characteristics that allow a peristaltic pump to move samples separated by a separation gas through the tube at a speed of at least 6 samples per minute without causing adjacent samples to mix with each other (see specification page 7, lines 28-31 and page 8, line 1). Thus the specification indeed provides a standard for ascertaining the requisite degree, and one of ordinary skill in the art would be reasonably apprised of the scope of the invention. Hence, this rejection is respectfully traversed with respect to the claims as currently presented.

With respect to claim 13, the indefiniteness in reciting “PVC” is obviated with respect to the claims as currently presented.

Claims 1-3, 5, 7-12, 15-19, and 26-27 stand rejected under U.S.C. 102(b) as being anticipated by Saros *et al.* (US 4,853,336). This rejection is respectfully traversed.

With respect to claim 1, Saros teaches a means for moving a plurality of samples and a means for introducing a separation gas between each of said plurality of samples. However, Saros fails to teach or suggest a means for selectively analyzing each of said plurality of samples for said particles in a flow cytometer as claimed in claim 1. The flow cytometer is an inherently different detector device than

those described by Saros. A flow cytometer is a pressurized device into which sample has to be pumped against pressure. Moreover, operation of a flow cytometer depends upon homogeneous, continuous sample flow for optimal performance. The use of a peristaltic pump to deliver samples to a flow cytometer in the present invention provides a homogeneous continuous sample flow. Saros does not teach or suggest the use of a peristaltic pump. Furthermore, a body of literature such as represented by Deandrade *et al.* and Zhi Z L (provided to the USPTO) suggests that bubbles disrupt the flow characteristics of the particles. Disruption of flow characteristics of the particles in the flow cytometer interferes with sample analysis. Therefore, previous applications in flow cytometry have involved removing bubbles from between the samples.

The present invention is contrary to conventional knowledge in the existing literature. We show that the flow cytometer of the present invention continues to function in an analytical capacity in the presence of bubbles inserted into the sample stream. The accompanying declaration states “experiments conducted in my laboratory indicate that integrity of the bubbles used to separate samples is important for proper sample separation in the flow cytometry apparatus of the present invention”. See page 2, declaration no 6 of Larry Sklar’s Declaration, under 37 C.F.R. § 1.32. Therefore the present claimed invention differs from the cited art. Hence, the rejection of claim 1 is respectfully traversed.

Claims 2-3, 5, 7-12, 15-19, and 26-27 are dependent on claim 1, and contain all the features of claim 1. Since Saros fails to teach all the elements of claim 1, Saros also fails to teach all the elements of claims 2-3, 5, 7-12, 15-19, and 26-27.

Claims 4, 2-3, 5, 7-12, 15-19, and 26-27 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Saros *et al.* in view of Kercso *et al.* (US 6,132,685) This rejection is respectfully traversed. Saros fails to teach or suggest all the elements of claim 1 and the claims dependent therefrom. Kercso fails to overcome the deficiencies of Saros. Hence, the rejection of claims 4, 2-3, 5, 7-12, 15-19, and 26-27 should be reconsidered and withdrawn.

Claim 25 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Saros *et al.* in view of Kercso *et al.* and in further view of Farrell *et al.* (US 5,788,927). This rejection is respectfully traversed. Saros fails to teach or suggest all the elements of claim 1 and the claims dependent therefrom. Kercso and Farrell both fail to overcome the deficiencies of Saros. Hence, the rejection of claim 25 should be reconsidered and withdrawn.

Claims 1-3, 8-12, 5-19, and 26-27 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Parce *et al.* (US 6,150,180) in view of Hach *et al.* or Trinel *et al.* (US 4,116,631). This rejection is respectfully traversed.

With respect to claim 1, Parce teaches a high throughput screening assay system in microscale fluidic devices. Parce teaches a means for moving a plurality of samples. Parce also teaches a means for introducing a separation plug of liquid between each of said plurality of samples. However, Parce fails to teach or suggest a means for introducing a separation gas between each of said plurality of samples and Parce also fails to teach a means for selectively analyzing each of said plurality of samples for said particles in a flow cytometer.

The flow cytometer is an inherently different detector device than the device described by Parce that is used to carry out biochemical enzymatic reactions in microchannels. The device used by Parce is a microfluidic device in which electronic pipettors are used to introduce samples into microchannels present on microchips. A plug of low ionic strength spacer fluid separates the samples in the system used by Parce. The samples on the microchips are moved in the system using electroosmotic fluid direction along with micropumps and microvalves.

Samples are introduced in the flow cytometer system of the present invention using an autosampler and air bubbles are used to keep the samples separate. A peristaltic pump is also used to move the samples in the flow cytometer of the present invention. These features are not taught by Parce, because Parce utilizes a detector device that differs in operation and function from a flow cytometer.

Hach teaches a method and apparatus for sampling impure water using automatic analyzers. Hach teaches a means for moving a plurality of samples. Hach also teaches a means for introducing a separation gas between each of said plurality of samples. However, the presence of air bubbles is detrimental to the functioning of the colorimetric detection cell, hence Hach teaches a method to get rid of the separation gas before the sample is detected.

In the present invention, a separation gas is specifically utilized to maintain the identity of multiple samples being analyzed. This feature is not taught by Hach. In fact, Hach teaches against using air bubbles during detection.

Hach also fails to teach a means for selectively analyzing each of said plurality of samples for said particles in a flow cytometer. Hence, Hach fails to overcome the deficiencies of Parce.

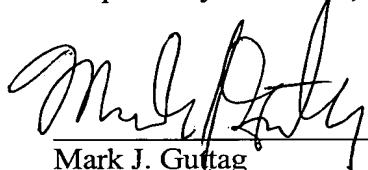
Trinel teaches a method for microbiological analysis of liquid mediums using a continuous flow analyzer. Trinel teaches a means for moving a plurality of samples. However, Trinel fails to teach a means for introducing a separation gas between each of said plurality of samples and also fails to teach or suggest a means for selectively analyzing each of said plurality of samples for said particles in a flow cytometer. Hence, Trinel also fails to overcome the deficiencies of Parce. Therefore, the rejection of claim 1 over Parce *et al.* (US 6,150,180) in view of Hach *et al.* or Trinel *et al.* (US 4,116,631) is improper. Thus Applicants respectfully request that the rejection be reconsidered and withdrawn.

Claims 2-3, 8-12, 5-19, and 26-27 are dependent on claim 1 and contain all the features of claim 1 and other features. As discussed above, Parce fails to teach or suggest all the elements of claim 1 and the claims dependent therefrom. Hach fails to overcome the deficiencies of Parce. Trinel fails to overcome the deficiencies of Parce. Therefore, the rejection of claim 2-3, 8-12, 5-19, and 26-27 over Parce *et al.* (US 6,150,180) in view of Hach *et al.* or Trinel *et al.* (US 4,116,631) is improper. Thus Applicants respectfully request that the rejection be reconsidered and withdrawn.

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In view of the foregoing, it is respectfully submitted that this application is now in condition for allowance, and favorable action is respectfully solicited.

Respectfully submitted,



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**ATTACHMENTS:**

**DECLARATION OF LARRY SKLAR**

**REQUEST FOR PRIORITY**

**ZHAO *et al.*, "A Flow Injection Flow Cytometry System for On-Line Monitoring of Bioreactors."**

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